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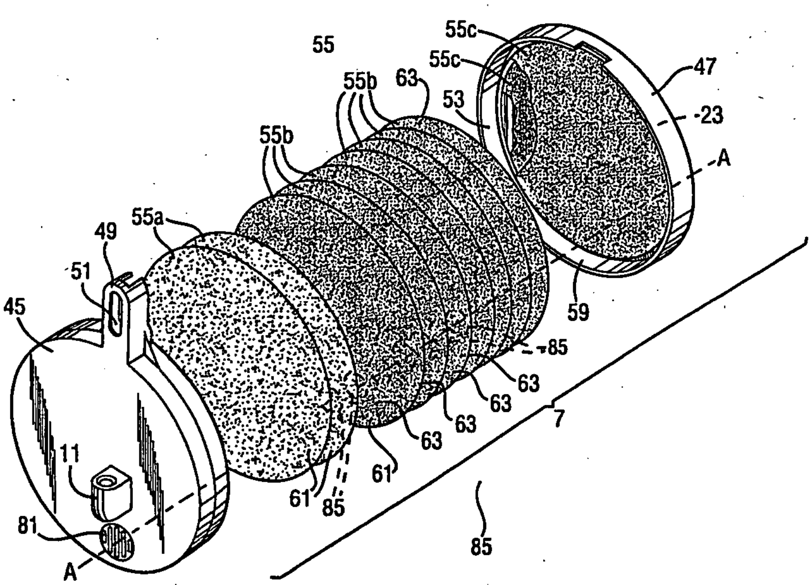

(57) Abstract: In one aspect of the invention a filter structure (55b, 57) for filtering a solid from a liquid (3) has a body which has an upstream outer surface (61, 65), a downstream outer surface (63, 67), is permeable to the liquid, is adapted to selectively filter the solid from the liquid on passage therethrough in a downstream direction, and is impermeable, or substantially impermeable, to a vent gas when wetted by the liquid. A section (85) of the body which extends from the upstream outer surface to the downstream outer surface is impermeable, or substantially impermeable, to the liquid and permeable to the vent gas so as to provide a pathway for the vent gas to pass in a downstream direction through the body. In a second aspect of the invention a filter sheet (55b) for filtering a solid from a liquid (3) has a body which has an upstream outer surface (61) and a downstream outer surface (63). A first section of the body extending from the upstream outer surface to the downstream outer surface is permeable to the liquid, adapted to selectively filter the solid from the liquid on passage therethrough in a downstream direction and impermeable, or substantially impermeable, to a vent gas when wetted by the liquid. A second section (85) of the body extending

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from the upstream outer surface to the downstream outer surface is impermeable, or substantially impermeable, to the liquid and permeable to the vent gas as to provide a pathway for the vent gas to pass in a downstream direction through the body. The filter structure or sheet thus incorporates means by which vent gas can pass to the downstream side of the filter structure or sheet and assist in recovery of the filtrate from the downstream side.

A FILTER

Field of the Invention

The present invention relates to a filter for filtering of a solid from a liquid, for instance filtering of leukocytes from blood to yield leukoreduced blood, and is particularly, although not exclusively, concerned with a process by which blood filters can be modified to enhance blood recovery.

Background of the Invention

Human blood transfusion that involves the transfer of donor leukocytes can be harmful to the patient. As an example, the donor leukocytes can give rise to febrile reactions or immune system suppression in the patient. The donor leukocytes can also result in the transmission of harmful infectious viruses to the patient, examples being human immunodeficiency virus (HIV), hepatitis, Epstein-Barr and cytomegalovirus. Moreover, blood transfusions involving the donor leukocytes can cause an immunological response in the patient which leads to future blood transfusions being rejected.

Consequently, it is preferable to filter the leukocytes from the donor's blood prior to its transfusion to the patient. That is to say, to effect blood transfusion with leukoreduced blood.

A typical blood filter device for yielding leukoreduced blood has a filter housing which defines a filter chamber which is divided into upstream and downstream sides by a blood filter membrane. An inlet port in the housing enables the donor blood to be conveyed into the upstream side and an outlet port enables the filtered blood to be conveyed from the downstream side to a collection bag. Blood filters by their nature are made of hydrophilic materials. Once filtration is complete, blood is recovered by allowing air into the upstream side of the filter housing. This air may potentially become contaminated. Moreover, whilst this technique allows the displacement of the upstream blood

volume, the filter membrane, being hydrophilic and coated in blood, resists the passage of air. The liquid can only be displaced with "considerable" pressure, air passing only when the bubble point pressure of the membrane is exceeded. This is impractical and potentially dangerous in clinical applications. Failure to completely drain blood filters leads to significant amounts of blood being lost to waste during both clinical transfusion and blood processing during the collection procedure.

In WO-A-9524255 (Hemasure, Inc.) there is disclosed a filter device for producing leukoreduced blood in which the hydrophilic multi-sheet filter membrane is apertured therethrough and an open-ended tube received in the aperture such that the tube open ends are respectively disposed in the upstream and downstream sides of the filter chamber. The upstream open end of the tube is closed by a hydrophobic filter whilst the downstream open end is left uncovered. The hydrophobic filter prevents blood passing from the upstream side to the downstream side through the tube. However, the hydrophobic filter permits the passage of air from the upstream side to the downstream side when the blood in the upstream side has receded sufficiently for the hydrophobic filter to be exposed. The air bubbles up through the leukoreduced blood in the downstream side to create a pressure head on the leukoreduced blood which displaces the leukoreduced blood out of the filter housing through the outlet port.

The filter device disclosed in WO-A-9524255 is highly complex, requiring close tolerances between the tube and the filter membrane, on the one hand, and the tube and the filter housing, on the other hand. If an ineffective seal is formed between the tube and the aperture in the filter membrane, donor blood can pass downstream into the downstream side with minimal leukoreduction. To combat this potential problem, highly complex mechanical solutions are needed.

It is an aim of the present invention in its broadest aspect to provide a filter for filtering a solid from a liquid which is provided with simpler means for allowing passage of a vent gas therethrough for promoting recovery of the filtrate.

It is also an aim of the invention according to one of its embodiments to provide an integral hydrophobic vent within the filter medium which will allow the passage of residual air from the collection (source) bag after processing, but not the passage of blood or other fluids during processing. This will facilitate complete drainage of both the proximal (upstream) and distal (downstream) portions of the filter and any attached administration set or downstream processing tubing without the need for excessive pressure or force. This process will reduce the amount of blood lost during administration and collection. Such a vent will permit the volume of air in the collection (source) bag, which is preferably equal to the known volume of blood in the filter and administration set, to drain the filter and administration set/downstream processing tubing, thereby maximising blood volume recovery/delivery.

Summary of the Invention

According to a first aspect of the present invention there is provided a filter structure for filtering a solid from a liquid having a body which:-
has an upstream outer surface,
has a downstream outer surface,
is permeable to the liquid,
is adapted to selectively filter the solid from the liquid on passage therethrough in a downstream direction, and
is impermeable, or substantially impermeable, to a vent gas when wetted by the liquid,
a section of the body which extends from the upstream outer surface to the downstream outer surface being impermeable, or substantially impermeable, to the liquid and permeable to the vent gas so as to provide a pathway for the vent gas to pass in a downstream direction through the body.

At least a portion of the section of the body may be impregnated with a material which renders that section of the body impermeable, or substantially impermeable, to the liquid and permeable to the vent gas.

The filter structure may be a single filter element or sheet or comprise a plurality of filter elements/sheets juxtaposed with one another.

According to a second aspect of the present invention there is provided a filter sheet for filtering a solid from a liquid having a body which has an upstream outer surface and a downstream outer surface, a first section of the body extending from the upstream outer surface to the downstream outer surface being permeable to the liquid, adapted to selectively filter the solid from the liquid on passage therethrough in a downstream direction and impermeable, or substantially impermeable, to a vent gas when wetted by the liquid, and a second section of the body extending from the upstream outer surface to the downstream outer surface being impermeable, or substantially impermeable, to the liquid and permeable to the vent gas so as to provide a pathway for the vent gas to pass in a downstream direction through the body.

By "substantially impermeable" is meant impermeable to a practical extent so that, in its context with reference to the vent gas, insufficient vent gas is able to pass through the wetted body or first section in the downstream direction to recover the filtrate and so that, in its context with reference to the liquid, sufficient vent gas is able to pass through the section or the second section for recovery of the filtrate. In other words, a deviation from absolute impermeability which does not prevent the invention performing its function.

The body of the filter structure and the first section of the filter sheet are impermeable, or substantially impermeable, to the vent gas when the filter structure body/first section is wetted by the liquid and the pressure of the vent gas is less than the bubble point pressure of the filter structure body/first section for the liquid. Conversely, the section of the filter structure and the second section of the filter sheet are permeable to the vent gas at this vent gas pressure.

The filter structure or sheet is preferably for filtering a solid from an aqueous liquid, more preferably for filtering cellular material from a body liquid and most preferably for filtering leukocytes from blood. The vent gas is typically air.

According to a third aspect of the present invention there is provided a filter device for filtering a solid from a liquid having a housing which defines a chamber and which has an inlet and an outlet to the chamber for the liquid and a filter structure according to the first aspect of the invention mounted in the chamber so that the upstream outer surface faces the inlet and the downstream outer surface faces the outlet.

According to a fourth aspect of the present invention there is provided a filter device for filtering a solid from a liquid having a housing which defines a chamber and which has an inlet and an outlet to the chamber for the liquid and a filter sheet according to the second aspect of the invention mounted in the chamber so that the upstream outer surface faces the inlet and the downstream outer surface faces the outlet.

Preferably, the housing of the filter device has a vent to the chamber for the vent gas to which the upstream outer surface faces towards.

The impregnated section of the filter structure may be made by chemical means as may be the second section of the filter sheet. For instance, in the case of the impregnated section of the filter structure, by applying the material to the body on one of the outer surfaces thereof and allowing the material to pass through the body to the other outer surface to impregnate or coat the body. The material is preferably applied in a liquid or vapour form, for example as one or more liquid droplets or in an aerosol formulation.

For filtering aqueous liquids, for instance blood, the impregnated section of the filter structure (when a single filter element) and the second section of the filter sheet are preferably an integral hydrophobic vent. An integral vent of this nature can be created by treating a small area of the filter medium chemically to create a hydrophobic channel, connecting the upstream and downstream portions of the filter chamber. Preferably, chemical insertion of a hydrophobic vent will involve the

use of a penetrative aerosol applicator of known design containing the hydrophobic chemical of known formula.

According to a fifth aspect of the present invention there is provided a hydrophobic vent designed for enhancing blood recovery during transfusion, collection or processing. The vent may be provided by chemical means. Such a vent will permit air to pass through and de-prime the filter and administration/processing tubing, increasing the volume of blood recovered after processing. The hydrophobic vent may be provided by applying a hydrophobic chemical to and through the filter medium using an aerosol applicator. Alternately, the hydrophobic vent may be provided by applying a hydrophobic chemical to and through the filter medium using a fluid dropper. The expanse of the hydrophobic vent may be limited by the shape of the nozzle of the applicator. The position and number of such vents is not limited in number or position. The system may be used in the processing of materials other than blood.

According to a sixth aspect of the invention there is provided a process for enhancing the recovery of blood when processing or administering it which consists of the introduction of a hydrophobic vent into the filter medium of the blood filter used during this procedure. This hydrophobic channel is chemical in structure. Chemical channelling is introduced by spraying a hydrophobic chemical onto and through a discrete section or sections of the filter medium. The hydrophobic channel permits the passage of air through the filter medium, thus permitting the filter to de-prime, enhancing the recovery of blood by the quantity of blood normally disposed of due to the inability to de-prime filters in the absence of a hydrophobic vent.

According to a seventh aspect of the invention there is provided a filter sheet for filtering a solid from an aqueous liquid having a body with an upstream outer surface and a downstream outer surface, the body having first and second sections extending from the upstream outer surface to the downstream outer surface, the first section being a hydrophilic filtering section and the second

section being a hydrophobic vent section. This filter sheet may replace the filter sheet in the filter device of the fourth aspect of the invention.

Within the context of the invention and its use for filtering blood, the term "hydrophilic" may be defined as meaning able to be wetted out so as to initiate and sustain bulk liquid flow under a pressure generated by a gravity head of approximately 1 m. Conversely, the term "hydrophobic" may be defined as meaning unable to wet out under pressure generated by a gravity head of approximately 1 m but which will allow air flow.

The terms "hydrophilic" and "hydrophobic" may also be defined using the concept of surface tension of liquids and the Critical Wetting Surface Tension (CWST) of a material. For a material to wet out, the CWST has to be greater than the surface tension of the liquid. Accordingly, a filter made from a material with a CWST greater than the surface tension of a blood preparation to be filtered will wet out and be classed as "hydrophilic". Conversely, a material with a CWST less than the surface tension of the blood preparation will not wet out and be classed as "hydrophobic". A typical blood (red cell) preparation has a surface tension of around 68-72 dynes/cm. In practice, the lower the CWST of the filter material vis-à-vis the surface tension of the blood preparation the better.

By way of example, the hydrophobic material for the hydrophobic section may be formed from a mixture of paraffin wax and an oleophobic hydrocarbon.

In accordance with the present invention, each aspect of the invention can be combined with one or more of the features of another aspect of the invention.

Further preferred features of the invention are set forth in the subsidiary claims appended hereto.

By way of example, a non-limiting embodiment of the present invention will now be described with reference to the accompanying Figures of drawings.

Brief Description of the Figures of Drawings

FIGURE 1 is a perspective view of a filtering apparatus comprising a filter device in accordance with the present invention;

FIGURE 2 is an exploded perspective view of the filter device showing the upstream and downstream halves of a filter housing of the filter device and the individual filter sheets contained therein:

FIGURES 3A and 3B are internal views of the upstream and downstream halves of the filter housing, respectively; and

FIGURES 4A and 4B are diagrammatic views of different stages of the operation of the filter device.

Detailed Description of an Exemplary Embodiment of the Invention

In FIGURE 1 there is shown a gravity-driven filtering apparatus 1 for filtering leukocytes from a source of donor blood preparation 3 contained in a sealed, sterile source bag 5 preparatory to transfusing the donor blood preparation 3 to a human patient. The donor blood preparation 3 is not whole blood. The blood plasma in the whole blood taken from the human donor is separated off by centrifuging and the cellular component of the whole blood, i.e. leukocytes, erythrocytes and thrombocytes, is typically added to an aqueous liquid such as the so-called 'optimal additive solution', or OAS for short, as is known in the art. There are occasions where OAS is not added to the red blood cells extracted from the donated whole blood, e.g. for paediatric use, when the patient cannot tolerate some of the components of the OAS and/or there is a need to keep the volume transfused as low as possible. Either way, it is this blood preparation derived from the donor's whole blood which is contained in the source bag 5. Typically, the source bag 5 will contain a volume of donor blood preparation 3 in the region of 350-400 ml.

The filtering apparatus 1 comprises a sterile, sealed filter device 7 having a transparent filter housing 9 having an internal chamber within which a filter media for filtering leukocytes from the donor blood preparation 3 is disposed, as will be described in more detail hereinafter. The filter housing 9 is provided with an inlet port 11 (see FIGURE 2) to which a downstream end of a sterile inlet tube 13 is sealably connected. An upstream end of the inlet tube 13 is sealably connected to a sterile hollow connector 15 having a sharp tip 17 which, when not in use, is covered by a sterile protective cap 19. Slidably mounted on the inlet tube 13 is an inlet clamp 21 having a clamping state which closes off the lumen of the inlet tube 13 and an unclamping state which leaves the lumen open.

In use, the protective cap 19 is removed from the connector 15 and the sharp tip 17 used to pierce a relatively short, closed outlet tube 22 located at the base of the source bag 5 and in fluid communication with the donor blood preparation 3. In this way, the connector 15 is sealably connected to the outlet tube 22. There are, of course, alternative ways of connecting the inlet tube 13 to the source bag 5, for example through Sterile Docking in which a machine called a Sterile Connecting Device (SCD™) heat welds inlet tube 13 to the outlet tube 22 on the source bag 5 whilst retaining sterility.

In addition to the inlet port 11, the filter housing 9 has an outlet port 23 to which an upstream end of a sterile outlet tube 25 is sealably connected. The outlet tube 23 has a downstream end which in turn is sealably connected to an inlet port 27 located at the top of a sealed, sterile collection bag 29 and in fluid communication with the interior thereof. Slidably mounted on the outlet tube 25 is an outlet clamp 31 which is adapted to close off and open the lumen of the outlet tube 25 in the same manner as the inlet clamp 21.

The top of the collection bag 29 is further provided with an outlet port 33 in fluid communication with the interior of the collection bag 29. An interior of a sterile satellite bag 35 is placed in fluid communication with the interior of the collection bag 29 through a sterile auxiliary tube 37 having its upstream end sealably connected to the outlet port 33 of the collection bag 29 and its

downstream end sealably connected to an inlet port 39 of the satellite bag 35 at the top thereof. As before, an auxiliary clamp 41 is slidably mounted on the auxiliary tube 37 to open and close the lumen thereof.

The filtering apparatus 1 operates as follows. Firstly, the individual clamps 21, 31, 41 are put into their clamping states so as to close off the lumens of the inlet, outlet and auxiliary tubes 13, 25, 37. The protective cap 19 is then removed from the connector 15 and the sharp tip 17 used to puncture the outlet tube 22 of the source bag 5 to place the inlet tube 13 in fluid communication with the donor blood preparation 3 in the source bag 5. The source bag 5 is then hung on a transverse bar of a stand (not shown) so that the filtering apparatus 1 is suspended from the stand. Preferably, the collection bag 29 is laid flat, e.g. on a base of the stand.

After suspension of the filtering apparatus 1, the inlet and outlet clamps 21, 31 are moved to their unclamping state whereby the donor blood preparation 3 is gravity-driven through the filtering device 7 and into the collection bag 29 via the inlet and outlet tubes 13, 25.

The conveyance of the donor blood preparation 3 through the filtering apparatus 1 into the collection bag 29 results in air contained in the inlet and outlet tubes 13, 25 and the filtering device 7 being conveyed into the collection bag 29. After the leukoreduced blood has been collected in the collection bag 29, the inlet and outlet clamps 21, 31 are returned to their clamping state, with the outlet clamp 31 being located in close proximity to the inlet port 27 of the collection bag 29. The auxiliary clamp 41 is then moved to its unclamping state and the collection bag 29 squeezed to express the air contained therein into the satellite bag 35 via the auxiliary tube 37. The auxiliary clamp 41 is then returned to its clamping state.

If desired, the collection bag 29 can be shaken gently and the auxiliary clamp 41 moved back to the unclamping state so that some of the leukoreduced blood is conveyed into the auxiliary tube 37. The auxiliary clamp 41 is then moved back to the clamping state and the tube 37 heat sealed at its opposed ends and at

positions intermediate the ends so as to give sealed tube segments containing samples of the leukoreduced blood. These samples can be analyzed to determine whether the donor blood preparation 3 has been leukoreduced to a sufficient degree for use in a blood transfusion.

After the donor blood preparation 3 has been filtered, the collection and satellite bags 29, 35 are separated from the rest of the filtering apparatus 1 which is disposed of. The auxiliary tube 37 and satellite bag 35 are then separated from the collection bag 29 to enable the collection bag 29 to be connected to a blood transfusion line through one or other of a pair of closed auxiliary outlet ports 43a, 43b on the collection bag 29, sample analysis permitting, of course.

Attention is now turned to FIGURES 2 to 4 for a more detailed explanation of the filtration of the donor blood preparation 3 in the filtering device 7. Referring first to FIGURE 2, it can be seen that the filter housing 9 has a transparent, cylindrical upstream half 45 and a transparent, cylindrical downstream half 47. The upstream and downstream halves 45, 47 are formed by injection moulding of a blood compatible plastics material, non-limiting examples being an acrylic plastic, such as acrylonitrile-butadiene-styrene (ABS), and polycarbonate.

The upstream and downstream halves 45, 47 have complementary outer circumferences which enable the halves 45, 47 to be connected by a push-fit. The connection of the outer circumferences of the upstream and downstream halves 45, 47 is sealed either through an O-ring (not shown), an adhesive seal or by welding. Other sealing methods could, of course, be adopted as will be understood by the person skilled in the art.

As shown in FIGURE 2, the upstream half 45 of the filter housing 9 is integrally formed with the inlet port 11 whereas the downstream half 47 is integrally formed with the outlet port 23. The upstream half 45 is also integrally formed with a projection 49 having an eyelet 51 through which the filter device 7 can be hung in position on the inlet tube 13, as shown in FIGURE 1.

As shown diagrammatically in FIGURES 4A and 4B, when the upstream and downstream halves 45, 47 of the filter housing 9 are connected together, a cylindrical filter chamber 53 is defined between them.

Disposed in the filter chamber 53 is a series of circular hydrophilic filter sheets 55a, 55b, 55c that are juxtaposed into a filter stack 57. The filter sheets 55a, 55b, 55c are sealably secured in place in the filter chamber 53 through a precision interference fit between the outer circumferences of the filter sheets 55a, 55b, 55c and an inner circumferential wall 59 of the filter chamber 53.

As will be understood from FIGURE 2, each filter sheet 55a, 55b, 55c has an upstream face 61 and a downstream face 63, with the upstream faces 61 facing the inlet port 11 and the downstream faces 63 facing the outlet port 23. As shown diagrammatically in FIGURES 4A and 4B, the outermost filter sheets 55a, 55c of the filter stack 57 present upstream 65 and downstream faces 67 of the filter stack 57. As further shown diagrammatically in FIGURES 4A and 4B, the filter stack 57 divides the filter chamber 53 into an upstream compartment 69, in fluid communication with the inlet port 11 and the upstream face 65 of the filter stack 57, and a downstream compartment 71, in fluid communication with the outlet port 23 and the downstream face 67 of the filter stack 57.

Referring to FIGURES 2, 4A and 4B, the filter stack 57 has 3 distinct stages, namely an upstream flow enhancement stage (FES) 72 consisting of the two outermost filter sheets 55a at the upstream end, a central leukocyte depleting stage (LDS) 74 consisting of the seven core filter sheets 55b and a downstream particle trap stage (PTS) 76 consisting of the two outermost filter sheets 55c at the downstream end.

The filter sheets 55a, 55b, 55c are of varying filtering grades, that is to say, the filter sheets 55a, 55b, 55c have different porosities. More particularly, the filter sheets 55a of the FES 72 have a larger mean pore size than the mean pore size of the filter sheets 55b, 55c of the LDS 74 and the PTS 76. Conversely, the filter sheets 55c of the PTS 76 have a smaller mean particle size than the mean pore

size of the filter sheets 55a, 55b of the FES 72 and LDS 74. In addition, the filter sheets 55a, 55c of the FES 72 and PTS 76 have a lower bubble point pressure than the filter sheets 55b of the LDS 74.

The FES 72 functions to remove gels and clots that may have formed in the donor blood preparation 3 which, if not removed, would block the finer filter sheets 55b of the LDS 74.

Preferably, the filter sheets 55b of the LDS 74 are of the same filtering grade, that is to say, have essentially the same mean pore size. However, the filter sheets 55b may be of different porosities, e.g. arranged so that the mean pore size in the LDS 74 decreases in the downstream direction. In any event, the mean pore size of the filter sheets 55b is such as to permit passage of erythrocytes whilst filtering leukocytes on downstream passage of the donor blood preparation 3 through the LDS 74.

The PTS 76 functions to filter out particles entrained in the donor blood preparation 3, e.g. foreign body particles picked up during the downstream passage of the donor blood preparation 3 through the FES 72 and/or the LDS 74. As an example, the PTS 76 may function to remove particles having a particle size of approximately 10 μm and above.

The filter sheets 55a of the FES 72 are preferably of a polyester which is modified to improve its wettability, i.e. to increase its Critical Wetting Surface Tension (CWST). The filter sheets 55b of the LDS 74 are preferably formed from glass microfibres, although other hydrophilic materials can, of course, be used, for instance a non-woven polyester such as polybutylene terephthalate (PBT) or polyethylene terephthalate (PET) surface-treated to increase its CWST, or a polyurethane etc.. Where the filter sheets 55b of the LDS 74 are made from glass, it is preferable for the filter sheets 55c of the PTS 76 to be of a non-glass material which is adapted to filter out any glass picked up by the donor blood preparation 3 on its passage through the filter stack 57.

Turning now to FIGURE 3A, the upstream half 45 of the filter housing 9 has an interior surface 73 in which the inlet port 11 opens and from which a series of baffles 75 project. The baffles 75 act to regulate and smooth the flow of the donor blood preparation 3 from the inlet port 11 into the upstream compartment 69 of the filter housing 9, in particular to cause the donor blood preparation 3 to spread. The upstream face 65 of the filter stack 57 is supported on the baffles 75.

From FIGURE 3B it can be seen that the downstream half 47 of the filter housing 9 has an interior surface 77 in which the outlet port 23 opens and from which a series of parallel ribs 79 project. The ribs 79 form a similar function as the baffles 75, namely to regulate and smooth the flow of the filtrate and to support the downstream face 67 of the filter stack 57.

As shown in FIGURES 2, 3A, 4A and 4B, the upstream half 45 of the filter housing 9 has an integrally formed air vent 81 adjacent the base thereof and lying on an axis A-A. As shown in FIGURE 3A, a hydrophobic membrane or cover 83 is mounted on the interior surface 73 of the upstream half 45 to cover the air vent 81, thereby preventing donor blood preparation 3 from discharging from the upstream compartment 69 through the air vent 81 while permitting the passage of air into the upstream compartment 69.

Turning attention back to FIGURE 2, each hydrophilic filter sheet 55b of the LDS 74 has a hydrophobic section 85 extending through its body from the upstream face 61 to the downstream face 63. The filter sheets 55b of the LDS 74 are arranged so that each hydrophobic section 85 is positioned on the axis A-A thereby being aligned with one another and with the air vent 81. In this way, a continuous hydrophobic channel 87 extends through the LDS 74 of the filter stack 57 from the upstream face 61 of the most upstream filter sheet 55b to the downstream face 63 of the most downstream filter sheet 55b, as shown diagrammatically in FIGURES 4A and 4B.

The hydrophobic channel 87 functions as a hydrophobic vent through which the donor blood preparation 3 is unable to permeate, at least to a significant

extent, but which, when uncovered by donor blood preparation 3, provides a pathway for air to pass from the upstream compartment 69 of the filter housing 9 to the downstream compartment 71, even though having been wetted by the donor blood preparation 3. In contrast, when the hydrophilic material of the filter sheets 55b of the LDS 74 is wetted by the donor blood preparation 3, the passage of air therethrough is prevented, unless the bubble pressure point of the filter sheets 55b is exceeded. The hydrophobic channel 87 thus enables the passage of air into the downstream compartment 71 of the filter housing 9 to assist in the recovery of the leukoreduced blood, as will be understood more clearly shortly hereinafter.

The bubble point pressure of the filter sheets 55a, 55c of the FES 72 and PTS 76 is such that the donor blood preparation 3 will clear from them under the pressure of the gravity head. Accordingly, it is not necessary for these filter sheets 55a, 55c to be provided with a hydrophobic section, although they may include it if desired, for example for manufacturing convenience.

The hydrophobic sections 85 of the filter sheets 55b are formed by impregnating the hydrophilic material in that section with a hydrophobic material. This may be done in a number of ways. As examples there may be mentioned the following:-

- Using a pipette or other such device to drop one or more liquid droplets of the hydrophobic material onto one of the upstream and downstream faces 61, 63 of the filter sheet 55b and allowing the hydrophobic material to penetrate into and through the filter sheet 55b to the opposite face.

- Spraying a hydrophobic chemical into and through the filter sheet 55b from an aerosol applicator. Over-spray can be prevented by the shape of the head or nozzle of the applicator.

- Grafting by irradiation, plasma or corona discharge, ion beam modification or chemical vapour deposition.

These processes result in the discrete section 85 of the hydrophilic material of the filter sheet 55b being coated in a hydrophobic material. For convenience, the hydrophobic sections 85 of the filter sheets 55b can be provided concurrently by stacking the untreated filter sheets 55b into the LDS 74 and then applying the hydrophobic chemical to either the upstream or downstream face of the stack so as to cause the chemical to penetrate into and through the stack to the opposite face. Another option would be to arrange all of the untreated filter sheets 55a, 55b, 55c into the filter stack 57 and then apply the hydrophobic chemical to either the upstream or downstream face 65, 67 of the filter stack 57 so as to cause the chemical to penetrate into and through the filter stack 57 to the opposite face. Obviously, in this case the hydrophobic channel 87 would extend through the FES 72 and PTS 76. Other ways of achieving the hydrophobic sections 85 on the filter sheets 55b will be apparent to the skilled person in the art.

The material of the hydrophobic section 85 has a Critical Wetting Surface Tension (CWST) which is less than the surface tension of the donor blood preparation 3 which is typically 68-72 dynes/cm. Preferably, the hydrophobic material has a CWST in the range of 19-67 dynes/cm, most preferably towards the lower end of this range. Preferably, the hydrophobic material has a CWST corresponding closely to that of polytetrafluoroethylene (PTFE), namely approximately 19-21 dynes/cm.

Attention is now directed to FIGURES 4A and 4B which diagrammatically illustrate the function of the hydrophobic channel 87 in the filter stack 57. FIGURE 4A shows the filter device 7 in an early stage of the filtering process in which the upstream compartment 69 of the filter housing 9 is filled to a level above the level of the axis A-A whereby the hydrophobic membrane 83 over the air vent 81 and the upstream end of the hydrophobic channel 87 are covered by the donor blood preparation 3. The donor blood preparation 3 permeates through the hydrophilic section of the filter stack 57 in a downstream direction, as indicated by the full-line arrows, and the resultant leukoreduced blood 89 is deposited in the downstream compartment 71 for discharge from the outlet port 23. However, the passage of

air through the filter stack 57 is prevented due to the hydrophilic material thereof being wetted by the donor blood preparation 3.

FIGURE 4B shows a terminal stage of the filtering process in which the level of the donor blood preparation 3 in the upstream compartment 69 has receded to expose the hydrophobic membrane 83 and the upstream end of the hydrophobic channel 87. As shown by the chain-line arrows, at this stage air at the ambient pressure of the local environment about the filter apparatus 1 (e.g. atmospheric pressure) passes through the air vent 81 and travels in a downstream direction through the filter stack 57, via the hydrophobic channel 87, into the downstream compartment 71 of the filter housing 9. The air bubbles up through the leukoreduced blood 89 to create a pressure head above it to promote its discharge from the outlet port 23. Thus, the amount of leukoreduced blood 89 recovered from the filter device 7 and downstream processing tubing 25 is increased compared to the case where no hydrophobic vent 87 is provided.

While it is preferable for the air vent 81 to be aligned with the hydrophobic channel 87, it is not strictly necessary. As an example, the air vent 81 could be located at a higher level than the hydrophobic channel 87. The air vent 81 could also be dispensed with and the air provided through the inlet tube 13, e.g. through use of an in-line air vent of the type disclosed in WO-A-9524255 *supra*.

As will be seen, the embodiment of the invention described hereinabove provides a simple solution to the problem of recovering leukoreduced blood from the downstream side of the filtering medium which can be readily adopted in existing filter devices since it does not require a new filter housing.

There now follows an Example of one way in which the hydrophobic sections 85 may be incorporated into the hydrophilic filter sheets 55b of the LDS 74 of the filter stack 57 as well as comparative test data showing the increased amount of leukoreduced blood 89 recovered with a filter arrangement of the invention.

Example

(a) Method

In this Example, a filtering apparatus 1 essentially as shown in FIGURE 1 was used with the following exceptions:-

- The filter stack 57 was hand assembled and sealed into the filter housing 9 using an O-ring and a clamp.

- 100 ml of a red cell blood preparation 3 was introduced into the source bag 5 via a 3-way tap cut into the inlet tube 13.

- ~~A drip chamber was introduced into the outlet tube 25 to increase the~~ downstream volume and thus enable any differences in blood recovery to be more clearly seen. By way of a more detailed explanation of this, the inlet and outlet tubes 13, 25 have a nominal inner diameter of 3 mm and a volume of approximately 0.07 cm^3 per 1 cm length. Using just tubing, the volume of the 1.25 m outlet tube 25 is only 8.75 cm^3. This is too small to reliably detect differences using the apparatus of FIGURE 1.

The head height of the filtering apparatus 1 as measured from the top of the 100 ml blood preparation 3 in the source bag 5 to the floor was set at 1.75 m with the inlet 11 to the filter device 7 being approximately 0.50 m from the initial blood level in the source bag 5.

The filter device 7 and the downstream section of the filtering apparatus 1 were primed with the blood preparation 3 so that there was a constant level of blood in the drip chamber and left to run until the drips entering the drip chamber stopped. Three filter runs were conducted with and without the filter sheets 55b in accordance with the invention and the net weight of leukoreduced blood 89 collected determined.

(b) Materials

For the filter runs using the invention, the LDS 74 was formed by 7 hydrophilic filter sheets 55b made from glass micro-fibre. Each filter sheet 55b (but not the filter sheets 55a, 55c of the FES 72 and PTS 76) was provided with a hydrophobic section 85 by placing 1 drop of a hydrophobic liquid onto it. Each hydrophobic section 85 was 9mm in diameter and placed using a template as close to the outer circumferential edge of the filter sheet 55b as possible. The filter sheets 55b were then placed by hand in the filter housing 9 together with the filter sheets 55a, 55c so that the hydrophobic sections 85 overlapped each other and lay on axis A-A (see FIGURES 2 and 4A).

The hydrophobic liquid used was a 80:20 volume/volume mixture of Repellan KFC™ and Repellan HY-N™ (both from Henkel Ltd). Repellan HY-N™ is a dispersion of fatty modified melamine derivative and paraffin. Repellan KFC™ is a perflouro alkyl acrylic co-polymer. One drop was placed, using a pipette, on each filter sheet 55b and the filter sheets 55b were then dried in an oven at 130°C for 5 minutes.

The Critical Wetting Surface Tension (CWST) of the hydrophobic sections 85 was determined to be 21 dynes/cm. This was in contrast to the hydrophilic glass micro-fibre zone whose CWST was in excess of 95 dynes/cm. The CWST is determined using liquids of different surface tensions and dropping a spot onto the surface to be tested. The surface tension of the liquid that does not soak into the filter is considered to be the CWST of the material.

The filter stack 57 used in the reference filter runs corresponded to that used for the example of the invention other than the filter sheets 55b of the LDS 74 not being provided with the hydrophobic section 85.

(c) Results

Once the source bag 5 had emptied of the blood preparation 3, the upstream chamber 69 of the filter device 7 in each test emptied as air entered from the atmosphere via the vent 81. For those filter devices 7 containing the filter sheets 55b provided with the hydrophobic section 85, air was seen in the outlet port 23 some 15-20 seconds after the upstream chamber 69 had emptied and this drained the downstream tubing 25 and the drip chamber. In contrast, once the upstream chamber 69 of the filter device 7 not having the hydrophobic-treated LDS 74 emptied of red cells, flow into (and out of) the downstream drip chamber ceased virtually immediately and the downstream volume did not drain.

The weight of the blood recovered in each filter run was determined and, as shown in the Table below, the inclusion of the hydrophobic section 85 in the filter sheets 55b resulted in an approximate 45% increase in the average weight of leukoreduced blood 89 recovered compared to the case where the hydrophobic section 85 was omitted.

Table

Amount of Recovered Leukoreduced Blood (grams)	With Hydrophobic Channel in LDS	Without Hydrophobic Channel in LDS
Sample 1	81.5	65.4
Sample 2	85.1	55.4
Sample 3	88.0	54.4
Mean	84.9	58.4
Standard Deviation	3.2	6.0

It will be understood that the present invention is not limited to the exemplary embodiment described above with reference to the accompanying FIGURES of drawings but may be varied or modified in many different ways within the scope of the appended claims. As an example, the process for chemical insertion of a hydrophobic vent into and through a filter medium can be applied to any single or multiple portion of the filter medium. Moreover, the invention in its broadest aspect is not restricted to blood filtration. For filtering aqueous liquids *per se*, the filter structure/sheet may be made by casting from Nylon®, a polyvinylidene fluoride (PVDF), a modified polyether sulphone (PES), cellulose acetate or mixed esters; or as a track etched membrane such a Cyclopore™ or Nuclepore™; or from non-woven fibres of e.g. polyester, polypropylene (PP) etc.; or from anodised alumina (Anopore™).

It will further be understood that the inclusion in the appended claims of reference numbers from the FIGURES of drawings is for illustration and not to be taken as having a limiting effect on the scope of the claims.

CLAIMS:

1. A filter structure (55b;57) for filtering a solid from a liquid (3) having a body which:-

has an upstream outer surface (61;65),

has a downstream outer surface (63;67),

is permeable to the liquid,

is adapted to selectively filter the solid from the liquid on passage therethrough in a downstream direction, and

is impermeable, or substantially impermeable, to a vent gas when wetted by the liquid,

wherein a section (85) of the body which extends from the upstream outer surface to the downstream outer surface is impermeable, or substantially impermeable, to the liquid and permeable to the vent gas so as to provide a pathway for the vent gas to pass in a downstream direction through the body.

2. A filter structure according to claim 1, wherein at least a portion (87) of the section of the body is impregnated with a material which renders the section of the body impermeable, or substantially impermeable, to the liquid and permeable to the vent gas.

3. A filter structure (57) according to claim 1 or 2 comprising a plurality of filter elements (55b) juxtaposed with one another.

4. A filter structure according to claim 3, wherein each filter element has a body with an upstream outer surface (61) and a downstream outer surface (63), the upstream and downstream outer surfaces of adjacent filter elements being juxtaposed to one another, wherein a section (85) of the body of each filter element which extends from the respective upstream outer surface to the respective downstream outer surface is impermeable, or substantially impermeable, to the liquid and permeable to the vent gas and wherein the filter elements are juxtaposed such that the section of the body of each filter element

overlaps the section of the body of each adjacent filter element to form the at least a portion (87) of the section of the filter structure (57).

5. A filter structure according to claim 2 or one of claims 3 and 4 when appended to claim 2, wherein the impregnated material is hydrophobic with respect to the body.

6. A filter structure according to any one of claims 1 to 5, wherein the body of the filter structure is hydrophilic.

7. A filter sheet (55b) for filtering a solid from a liquid (3) having a body which has an upstream outer surface (61) and a downstream outer surface (63), wherein a first section of the body extending from the upstream outer surface to the downstream outer surface is permeable to the liquid, adapted to selectively filter the solid from the liquid on passage therethrough in a downstream direction and impermeable, or substantially impermeable, to a vent gas when wetted by the liquid, and wherein a second section (85) of the body extending from the upstream outer surface to the downstream outer surface is impermeable, or substantially impermeable, to the liquid and permeable to the vent gas so as to provide a pathway for the vent gas to pass in a downstream direction through the body.

8. A filter sheet according to claim 7, wherein the second section is hydrophobic with respect to the first section.

9. A filter sheet according to claim 7 or 8, wherein the first section is hydrophilic.

10. A filter structure or sheet according to any one of the preceding claims for filtering a solid from an aqueous liquid.

11. A filter structure or sheet according to any one of the preceding claims for filtering cellular material from a body liquid.

12. A filter structure or sheet according to claim 11 for filtering leukocytes from blood.

13. A filter structure or sheet according to any one of the preceding claims, wherein the vent gas is air.

14. A filter structure or sheet according to any one of the preceding claims, wherein the section or the second section is located towards, or adjacent, an outer perimeter of the filter structure or sheet.

15. A filter structure (57) comprising a plurality of the filter sheets according to any one of claims 7 to 14 juxtaposed with one another so that the upstream and downstream outer surfaces of adjacent filter sheets are juxtaposed to one another and so that the second section of the body of each filter sheet overlaps the second section of the body of each adjacent filter sheet.

16. A filter device (7) for filtering a solid from a liquid (3) having a housing (9) which defines a chamber (53) and which has an inlet (11) and an outlet (23) to the chamber for the liquid and a filter structure (55b;57) according to any one of claims 1 to 6 or 10 to 14 mounted in the chamber so that the upstream outer surface faces the inlet and the downstream outer surface faces the outlet.

17. A filter device (7) for filtering a solid from a liquid (3) having a housing (9) which defines a chamber (53) and which has an inlet (11) and an outlet (23) to the chamber for the liquid and a filter sheet (55b) according to any one of claims 7 to 14 mounted in the chamber so that the upstream outer surface faces the inlet and the downstream outer surface faces the outlet.

18. A filter device according to claim 16 or 17, wherein the housing has a vent to the chamber for the vent gas and wherein the upstream outer surface faces the vent.

19. A filter device according to claim 18, wherein when the housing is held upright the vent is located no lower than the section of the filter structure or the second section of the filter sheet.

20. A filter device according to claim 18 wherein the vent is in alignment with the section of the filter structure or the second section of the filter sheet.

21. A filter device according to any one of claims 16 to 20, wherein the section or the second section is located adjacent the perimeter of the chamber.

22. A filter device according to claim 21, wherein in an upright orientation of the housing the section or the second section is adjacent the bottom of the chamber.

23. A filter device according to claim 17 or any one of claims 18 to 22 when appended to claim 17 in which the filter sheet forms the most upstream filter sheet of the filter structure of claim 15.

24. A method of fabricating a filter structure (55b;57) according to claim 2 or any one of claims 3 to 6 or 10 to 14 when appended to claim 2 comprising the steps of applying the material to the body on one of the outer surfaces (61,63;65,67) thereof and allowing the material to pass through the body to the other outer surface to impregnate the body.

25. A method according to claim 24 in which the material is applied in a liquid or vapour form.

26. A method according to claim 24 in which the material is applied to the outer surface as one or more liquid droplets.

27. A method according to claim 24 in which the material is applied to the outer surface in an aerosol formulation.

28. A method of filtering a blood component from blood comprising the steps of passing the blood through a filter structure or filter sheet according to any one of claims 1 to 15 in a downstream direction.

29. Blood obtained from the method according to claim 28.

30. A filter structure or sheet substantially as hereinbefore described with reference to, and as illustrated by, the accompanying FIGURES of drawings.

31. A filter device substantially as hereinbefore described with reference to, and as illustrated by, the accompanying FIGURES of drawings.

32. A method of forming a filter structure or sheet substantially as hereinbefore described with reference to, and as illustrated by, the accompanying FIGURES of drawings.

33. A method of filtering a blood component from blood substantially as hereinbefore described with reference to, and as illustrated by, the accompanying FIGURES of drawings.

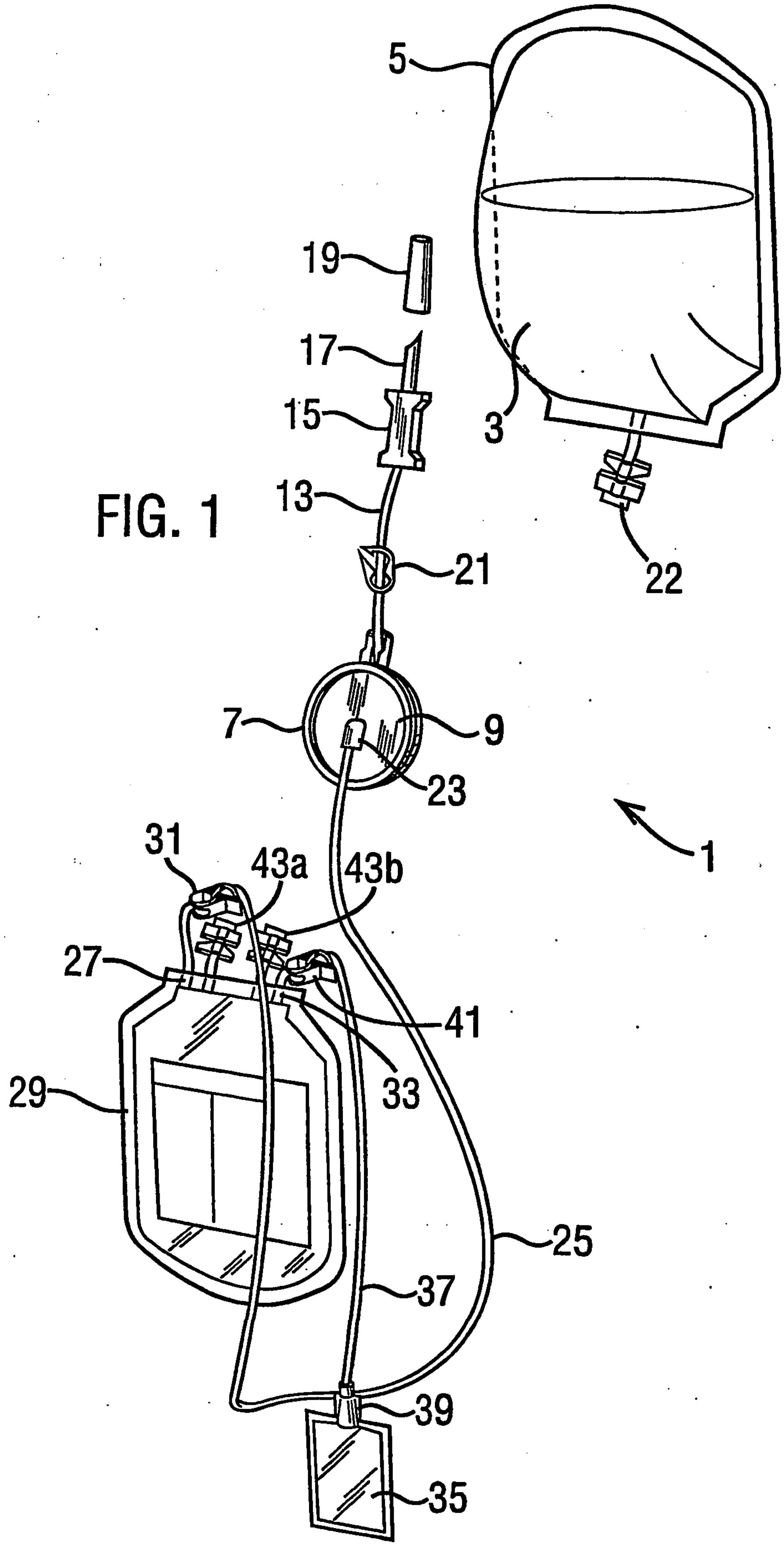

FIG. 1

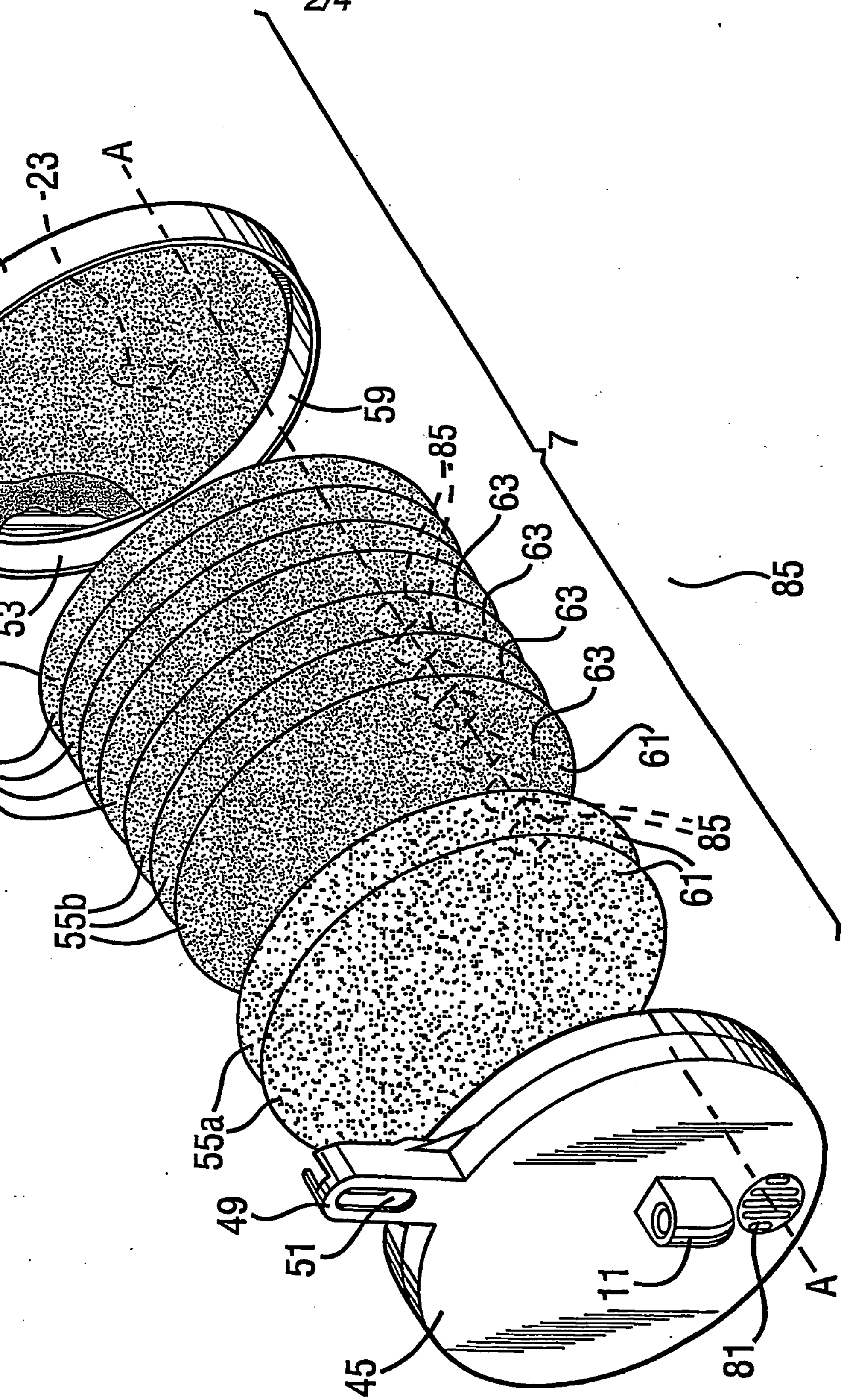
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FIG. 2

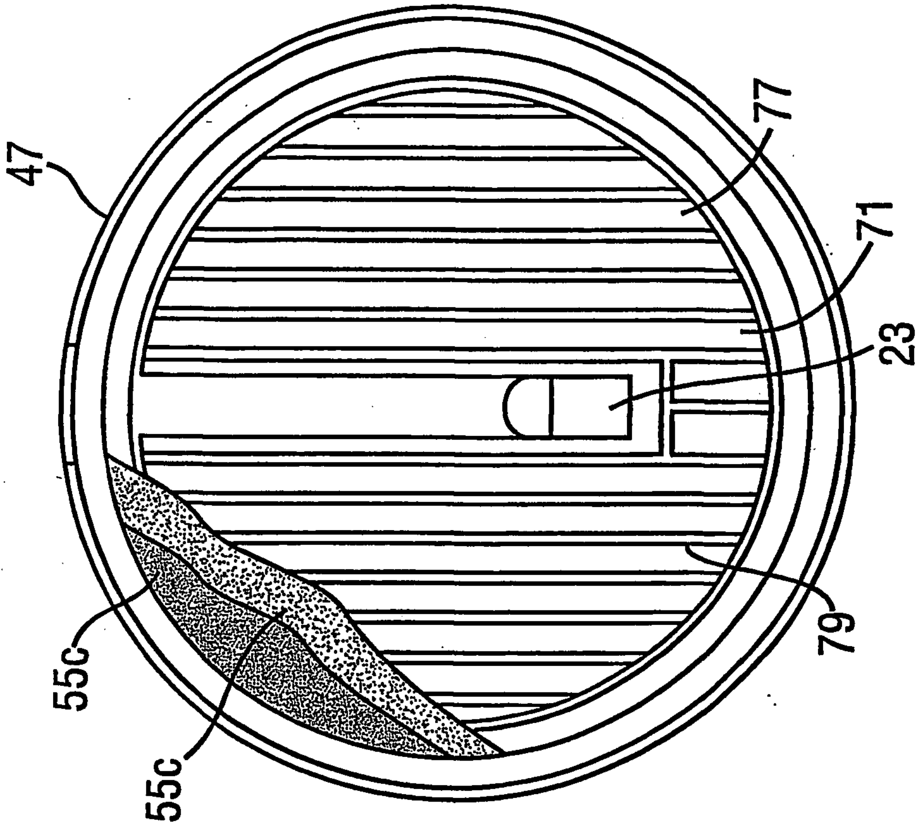

FIG. 3B

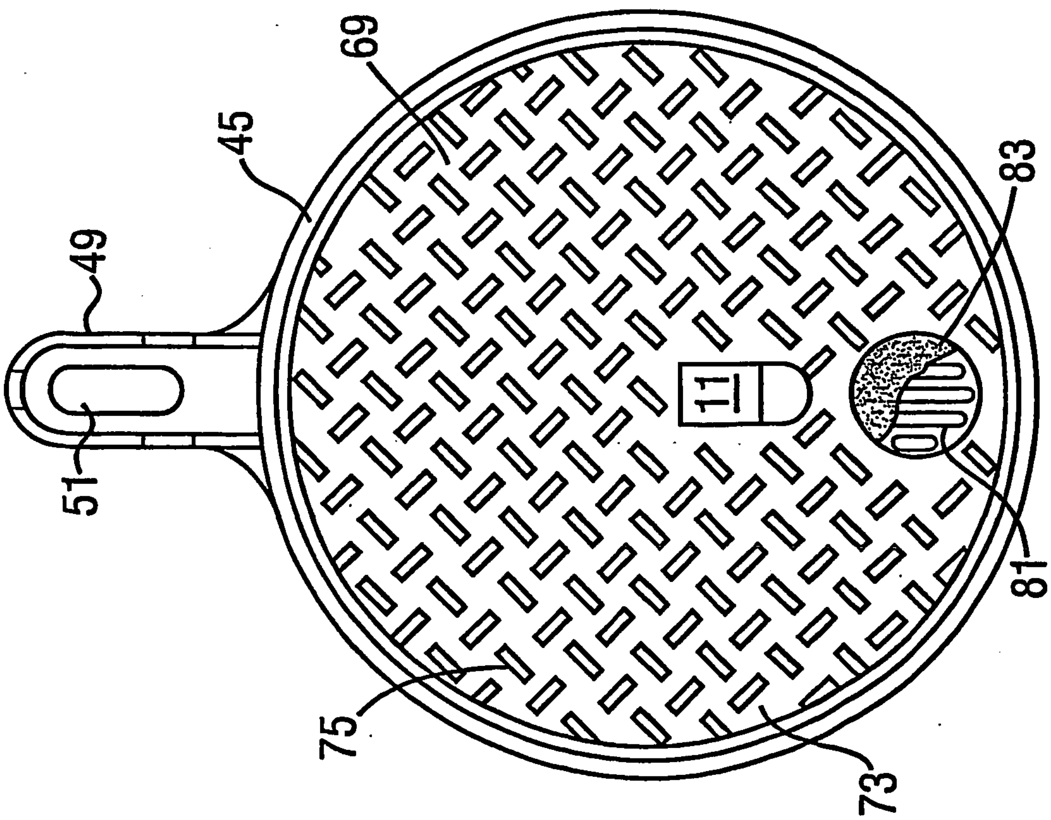

FIG. 3A

FIG. 4A

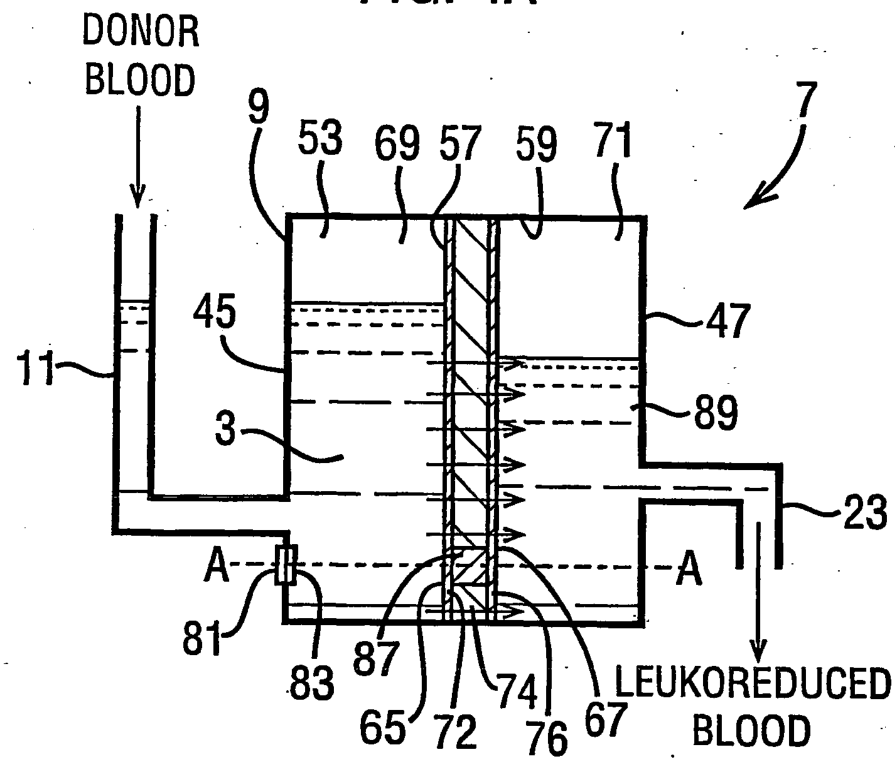
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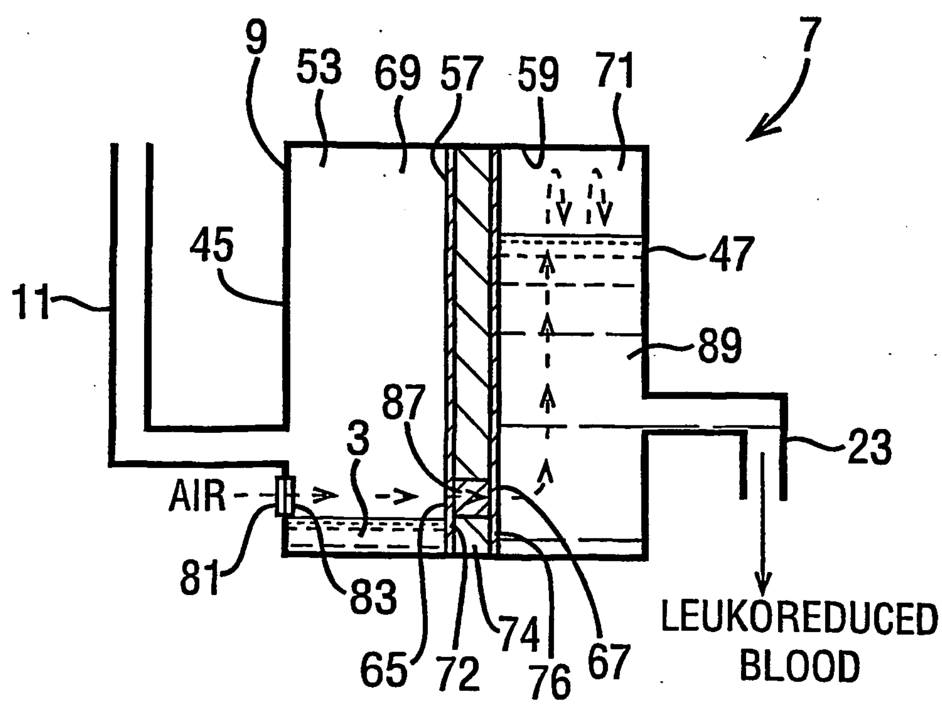
FIG. 4B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INTERNATIONAL SEARCH REPORT

In ›nal Application No
PL., ıB 01/03474

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01D36/00 A61M1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01D A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 17369 A (PALL CORP ;EVANS NOEL A (US); PASCALE FRANK R (US); RONAN JOHN B () 30 April 1998 (1998-04-30)	1,2, 5-13, 16-18, 28,29
Y	page 6, line 15 -page 8, line 7	3,4,14, 15,19-23
	page 14, line 10 - line 32 page 19, line 11 - line 13 ---	
X	US 3 520 416 A (KEEDWELL CYRIL A) 14 July 1970 (1970-07-14)	1-11,13, 24-27
Y	column 1, line 27 -column 4, line 54; example 3 ---	14
Y	US 5 472 605 A (ZUK JR PETER) 5 December 1995 (1995-12-05) cited in the application abstract; figure 2 -----	3,4,14, 15,19-23

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 October 2001	08/11/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Péru, L

INTERNATIONAL SEARCH REPORT

formation on patent family members

In ...nal Application No
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